DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendments 25 September 2006 and 17 May 2010 of 20 November 2004 have been entered in full. Claim 28 is amended. Claims 31-47 are added. Claims 1-27 are cancelled.

It is noted that new claims 35 and 43 do not have a status identifier. Since these claims were added in the amendment of 17 May 2010, the status identifiers should have recited "New". Furthermore, the claim listing of 17 May 2010 indicates that claims 1-28 are cancelled and claim 28 is amended, while Applicant's comments in response to the Restriction requirement indicate that claims 1-27 are cancelled. On March 22, 2011, Applicant's representative, Donna Perdue, stated that claims 1-27 are cancelled and claim 28 is amended (please see Interview Summary attached to the instant Office Action).

Election/Restrictions

Applicant's election of Group VII, claims 28-30, directed to a method of extracorporeal manipulation, depletion, and/or removal of soluble suspended components or cellular blood components, in the reply filed on 17 May 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election of antibody fragment as the species of Component C in the reply filed on 17 May 2010 is also acknowledged.

Claims 46 and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 May 2010.

Claims 28-45 are under consideration in the instant Office Action.

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the citizenship of each inventor.

Sequence Compliance

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). **Specifically, the sequences disclosed in Figures 19-26 are not accompanied by the required reference to the relevant sequence identifiers. Additionally, the specification discloses sequences at page 15 (lines 19-20), page 16 (line 27), page 41 (lines 7-8), page 48 (lines 30-31), page 49 (lines 1-2), pages 59-60, page 62, and page 64 that are not accompanied by the required reference to the relevant sequence identifiers.** This application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Please also see the PTO-90C and Revised Notice to Comply forms attached to the instant Office Action.

Drawings

4. The drawings are objected to because the instant drawings do not comply with 37 C.F.R. § 1.84(U)(1), which states that partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. Figure 19 of the instant application, for example, is presented on 2 separate panels/sheets. The two total sheets of drawings for Figure 19 should be renumbered "Figures 19A-19B". Figures 20-26 are also shown on 2 or more sheets. The multiple sheets for Figures 19-26 should be renumbered with the Figure number, followed by a capital letter (i.e., A, B, C, etc.).

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Applicant is reminded that once the drawings are changed to meet the separate

numbering requirement of 37 C.F.R. 1 1.84(U)(1), Applicant is required to file an amendment to change the Brief Description of the Drawings and the rest of the specification accordingly.

Specification

5. The disclosure is objected to because of the following informalities:

5a. The specification of the instant application does not contain any headings.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Appropriate correction is required.

Claim Objections

6. Claims 28-45 are objected to because of the following informalities:

6a. Claim 28, line 1, should be amended to recite "A method for extracorporeal manipulation…" rather than "Method for extracorporeal manipulation…".

6b. In claim 32, line 1, the word "stem" should be amended to recite for example, "are".

6c. In claim 33, line 2, the comma after the word "group" should be deleted.

6d. In claim 40, line 1, the word "stem" should be amended to recite for example, "are".

6e. Claims 29-45, line 1, should be amended to recite "The method according to claim...".

Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 28-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 28-45 are indefinite because the elements recited in the claim do not constitute proper Markush groups. The claims are indefinite in the alternative use of "and/or" because it is not clear what controls which of these limitations. See MPEP § 2173.05(h). Please see for example, claim 28 (lines 1, 4, 10).

9. Regarding claims 28-45, claim 28 recites the limitation "the blood" in lines 3, 6, 13. There is insufficient antecedent basis for this limitation in the claim. Claim 28 does not recited "blood" before line 4. The preamble of the claim only recite "cellular blood components".

10. Claim 30 recites the limitation "the thus treated blood or blood fraction" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 28, from which claim 30 depends, does not have a specific limitation or step reciting the treatment of blood or blood fraction.

11. Claim 30 is rejected as being indefinite because the phrase "blood or blood fraction is reinjected into a patient" is not clear. First, claim 28, from which claim 30 depends, does not recite that a blood or blood fraction is removed from a patient. Second, even if it did, would the blood or blood fraction be administered to the same patient or a different patient. Finally, it is also not clear how many times the blood or blood fraction is injected into a patient because claim 30 recites the term "reinjects". This term means "inject again".

12. Claim 43 recites the limitation "on the cell surface" in line 3. There is insufficient antecedent basis for this limitation in the claim. Claim 28, from which claim 43 depends, does not recite the terms "cell" or "cell surface".

13. Claims 28-45 are rejected as being indefinite because the preamble of claim 28 is not clear and concise. Claim 28 recites a "method for extracorporeal manipulation, depletion, and/or removal of soluble, suspended components or cellular blood components". Hence, it is not clear what the soluble, suspended components are being manipulated, depleted, or removed from. Blood? Urine? Buffer?

14. Claims 28-45 are rejected as being indefinite because claim 28 does not have a step that clearly relates back to the preamble. For example, steps (a) and (c) of claim 28 are optional. Step (b), which is directed to binding, is the only required step. Hence, there is no clear step indicating the extracorporeal manipulation, depletion, and/or removal of soluble, suspended components or cellular blood components (i.e., the goal of the preamble).

15. Regarding claims 41, 44, and 45, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in Ex parte Wu, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of Ex parte Steigewald, 131 USPQ 74 (Bd. App. 1961); Ex parte Hall, 83 USPQ 38 (Bd. App. 1948); and Ex parte Hasche, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 41 recites the broad recitation “N-terminal tag sequence”, and the claim also recites “particularly a His tag sequence or a Flag tag sequence” which is the narrower statement of the range/limitation. In the present instance, claim 44 recites the broad recitation “an antibody fragment from a mammal”, and the claim also recites “particularly of murine or human origin, or a humanized antibody fragment” which is the narrower statement of the range/limitation. In the present instance, claim 45 recites the broad recitation “different antibody formats”, and the claim

also recites "e.g., as scFV, particularly scFv40" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 28-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 28 is directed to a method for extracorporeal manipulation, depletion, and/or removal of soluble, suspended components or cellular blood components, comprising: (a) optional separation of the blood into one or more fractions with solid and/or liquid components; (b) binding of soluble, suspended, or cellular blood components of the blood to a surface or particle coupled to a polypeptide wherein the polypeptide comprises at least three components A and at least two components B, wherein each component A is a monomer of a member of the TNF ligand family or a functional fragment and/or a functional variant thereof, and each component B is a peptide linker; and (c) optional separation of the bound soluble, suspended, or cellular blood components of the blood. Claim 31 recites that components A are identical or different. Claim 32 recites that components A stem from the same organism or different organisms.

(i) The specification of the instant application teaches that the invention relates to methods for extracorporeal (ex vivo) manipulation, depletion, and/or removal of components present in body fluids, such as, e.g. binding partners of a component A, as defined above, or cells binding thereto or associated therewith (page 27, lines 9-12). The specification also discloses that such extracorporeal methods comprise preferably such methods as, e.g., apheresis, particularly the basic forms of apheresis, plasmapheresis and cytapheresis (page 27, lines 12-13). The specification teaches the generation of single chain TNF (scTNF) proteins that differ in the length of the peptide linker between the three individual TNF modules (pages 40-41; Figures 1-3; page 56, lines 13-19). The specification also discloses the covalent coupling of reduced CysHis-scTNF to silica microparticles (beads) (bottom of page 64 through the top of page 65). However, there are no methods or working examples in the instant specification that indicate the binding of soluble, suspended or cellular blood components to a surface/particle coupled to a polypeptide comprising at least three components A and at least two components B, wherein each component A is a monomer of a member of the TNF ligand family or a functional fragment and/or a functional variant thereof, and each component B is a peptide linker. It is not clear from the claims and the instant specification what cellular blood components would be bound and separated by the claimed method. For instance, there is no requirement that the blood components express a TNF receptor. The phrase "soluble, suspended cellular blood or cellular blood components" is extremely broad, encompassing not only cells themselves, but also, for example, fat, cell debris, hormones, carbohydrates, and proteins. It is not clear how the claimed method of utilizing a polypeptide comprising at least three components A and at least two components B would bind soluble, suspended cellular blood or cellular blood components, such

as fat, cell debris, hormones, carbohydrates, and proteins. Furthermore, there are also no methods or working examples that indicate the separation of the bound, suspended, or cellular blood components. The specification does not disclose that treated blood or blood fraction is injected or reinjected into a patient. It is not clear why the treated blood or blood fraction would be injected or reinjected into a patient. Hence, a large quantity of experimentation would be required of the skilled artisan to bind soluble, suspended or cellular blood components to a surface/particle coupled to a polypeptide comprising at least three components A and at least two components B; separate the bound, suspended, or cellular blood components; and inject or reinject treated blood or a blood fraction into a patient. Such experimentation is considered undue.

Additionally, the specification teaches the generation of scTNF, scFasL, scTRAIL (Figures 19-26; pages 49-54). Specifically, Figures 19, 20, 23, and 26 (pages 49-50, 52, 54) disclose a construct with three identical TNF modules (amino acids 79-181 of human TNF). Figures 21 and 24 (page 51 and 52-53) teach a construct with three identical FasL modules (amino acids 139-281 of human FasL). Figures 22 and 25 (pages 51-52; 53-54) disclose a construct with three identical TRAIL modules (amino acids 95-281 of human TRAIL). However, the claimed method recites that the polypeptide bound to a surface or particle comprises at least three components A, wherein each component A is a monomer of a member of the TNF ligand family. Claim 31 recites that the components A are identical or different and claim 32 recites that the components A are from the same or different organisms. Thus, the three components A can be from different TNF ligand family members (i.e., FasL, TRAIL, and TNF, etc.), can be any length or sequence (see part (ii) below), and can be from any species.

However, the specification does not teach any methods or working examples that indicate different TNF ligand family monomers (and even different species of TNF ligand family monomers) together generate a functional single chain monomer protein. There are over 15 TNF ligand family members known in the art. Yet, there is little or no guidance in the specification indicating that the TNF ligand family members (and different species of the members) would be interchangeable with one another in a polypeptide that comprises at least three, and potentially more, members. One skilled in the art would not be able to predict that all possible permutations of the polypeptide encompassed by the instant claims would have the desired activity and a large quantity of experimentation would be required of the skilled artisan to determine such. Such experimentation is considered undue.

(ii) The specification of the instant application teaches that a polypeptide or a component A or a fragment or variant thereof is functional within the meaning of the invention, provided it exhibits its biological activity of function (page 6, lines 20-21). The specification discloses that "[i]n the case of functional fragments and the functional variants of the invention, these biological functions can in fact be changed, e.g., with respect to their specificity or selectivity, but with retention of the basic biological function" (page 6, lines 23-26). The specification teaches that the fragment of a monomer represents its extracellular domain, which corresponds to the entire extracellular domain of the soluble wild-type member of the TNF ligand family or a segment thereof (page 7, lines 12-24). The specification also teaches that "[i]n particular, monomers, polypeptide, or proteins, or fragments thereof that have sequence differences relative to the corresponding native sequences are designated as variants of biologically active monomers, polypeptides, or proteins, or fragments thereof, or a component A…These sequence

deviations can be one or more insertion(s), deletion(s), and/or substitution(s) of amino acids, whereby there is a sequence homology of at least 60%, preferably 70%, more preferably 80%, also more preferably 85%, even more preferably 90%, and most preferably 97%" (page 8, lines 4-11). However, the specification does not enable all possible TNF ligand family monomer fragments and variants with a biological activity (as component A) other than the wild-type (non-mutated) extracellular domains of TNF ligand family members. The specification also does not teach any functional or structural characteristics of the monomer variants, fragments, and derivatives recited in the claims.

The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein segments which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and

extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Additionally, the monomer fragments and variants utilized in the claimed method do not require a specific function. Relevant literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities. For example, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48). Halkier et al. (US 2004/0014948) teach a single-chain oligomeric TNF-α polypeptides that are modified and behave as partial TNF-α agonists, competitive TNF-receptor antagonists, and partial antagonists (pages 24-25, [0256]; pages 27-29; Example 2, pages 39-40). Desjarlais et al. (US Patent 7,662,367) disclose variant TNF-α proteins that interact with the wild-type TNF-α to form mixed trimers incapable of activating receptor signaling (column 4, lines 34-65). Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the

art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the monomer fragments and variants in the claimed method without resorting to undue experimentation to determine what the specific biological activities of the fragments and variants are.

Due to the large quantity of experimentation necessary to generate the infinite number of monomer fragments and derivatives recited in the claims and possibly screen same for activity; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and that biological activity cannot be predicted based on structural similarity; and the breadth of the claims which fail to recite any specific structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

17. Claims 28-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 28 is directed to a method for extracorporeal manipulation, depletion, and/or removal of soluble, suspended components or cellular blood components, comprising: (a) optional separation of the blood into one or more fractions with solid and/or liquid components;

(b) binding of soluble, suspended, or cellular blood components of the blood to a surface or particle coupled to a polypeptide wherein the polypeptide comprises at least three components A and at least two components B, wherein each component A is a monomer of a member of the TNF ligand family or a functional fragment and/or a functional variant thereof, and each component B is a peptide linker; and (c) optional separation of the bound soluble, suspended, or cellular blood components of the blood. Claim 31 recites that components A are identical or different. Claim 32 recites that components A stem from the same organism or different organisms.

The specification of the instant application teaches that a polypeptide or a component A or a fragment or variant thereof is functional within the meaning of the invention, provided it exhibits its biological activity of function (page 6, lines 20-21). The specification discloses that "[i]n the case of functional fragments and the functional variants of the invention, these biological functions can in fact be changed, e.g., with respect to their specificity or selectivity, but with retention of the basic biological function" (page 6, lines 23-26). The specification teaches that the fragment of a monomer represents its extracellular domain, which corresponds to the entire extracellular domain of the soluble wild-type member of the TNF ligand family or a segment thereof (page 7, lines 12-24). The specification also teaches that "[i]n particular, monomers, polypeptide, or proteins, or fragments thereof that have sequence differences relative to the corresponding native sequences are designated as variants of biologically active monomers, polypeptides, or proteins, or fragments thereof, or a component A…These sequence deviations can be one or more insertion(s), deletion(s), and/or substitution(s) of amino acids, whereby there is a sequence homology of at least 60%, preferably 70%, more preferably 80%,

also more preferably 85%, even more preferably 90%, and most preferably 97%" (page 8, lines 4-11).

The claims of the instant application do not require that the functional fragment or functional variant of a monomer of a member of the TNF ligand family possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of proteins and methods of using such. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include actual reduction to practice, disclosure of drawings or structure chemical formulas, sufficient relevant identifying characteristics (such as, complete or partial structure, physical and/or chemical properties, and functional characteristics when coupled with a known or disclosed structure/function correlation), methods of making the claimed product, level of skill and knowledge in the art, predictability in the art, or any combination thereof. However, in this case, the specification fails to disclose and there is no art-recognized correlation between the structure of the genus of functional fragments or functional variants of a monomer of a member of the TNF ligand family and a function. The specification does not teach which amino acids can vary from the full-length (wild-type) or extracellular domain of a TNF ligand family member and still result in a protein that retains a specific activity. Therefore, the description of full-length and extracellular domains of TNF ligand family members (page 11, lines 12-27) is not adequate written description of an entire genus of functional fragments or functional variants of a monomer of a member of the TNF ligand family and a function.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See Vas-Cath at page 1116).

Thus, the skilled artisan cannot envision the detailed chemical structure of the protein fragments and variants of the encompassed claims and methods of using such, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The proteins are required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only full-length and extracellular domains of TNF ligand family members (as component A) and methods of using such, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Krippner-Heidenreich et al. J Immunol 180(12): 8176-8183, 2008 (teachings of the instant specification)

Klysner et al. US 2003/0185845 (teach TNF monomerized trimer constructs; page 20, Example 8)

Tovar et al. U.S. Patent 7,368,295 (TNF trimer immobilized on nanoparticles; columns 25-27)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571)272-0881. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
23 March 2011

/Bridget E Bunner/
Primary Examiner, Art Unit 1647